General

Guideline Title

ACR Appropriateness Criteria® Hodgkin lymphoma—unfavorable clinical stage I and II.

Bibliographic Source(s)

Roberts KB, Younes A, Hodgson DC, Advani R, Dabaja BS, Dhakal S, Flowers CR, Ha CS, Hoppe BS, Mendenhall NP, Metzger ML, Plastaras JP, Shapiro R, Smith SM, Terezakis SA, Winkfield KM, Constine LS, Expert Panel on Radiation Oncologyâ€“Lymphoma. ACR Appropriateness CriteriaÂ® Hodgkin lymphoma - unfavorable clinical stage I and II. Reston (VA): American College of Radiology (ACR); 2015. 22 p. [83 references]

Guideline Status

This is the current release of the guideline.

This guideline updates a previous version: Das P, Ng A, Constine LS, Advani R, Flowers C, Friedberg J, Hodgson DC, Schwartz CL, Wilder RB, Wilson LD, Yunes MJ, Expert Panel on Radiation Oncology-Hodgkin's Lymphoma. ACR Appropriateness Criteria® Hodgkin's lymphoma - unfavorable clinical stage I and II. [online publication]. Reston (VA): American College of Radiology (ACR); 2010. 6 p. [24 references]

This guideline meets NGC's 2013 (revised) inclusion criteria.

Recommendations

Major Recommendations

ACR Appropriateness Criteria®

Clinical Condition: Hodgkin Lymphoma — Unfavorable Clinical Stage I and II

Variant 1: 45-year-old man with stage IIA nodular sclerosis Hodgkin lymphoma (NSHL); supradiaphragmatic (involving bilateral neck and mediastinum), no bulky disease; ESR, 55.

Treatment	Rating	Comments
Overall plan		
Combined modality therapy	9	
Chemotherapy alone	6	Chemotherapy alone might be considered if there is high cardiovascular risk or contraindications to RT.
RT alone	2	
Rating Scale: 1,2,3 Usually not appropriate; 4,5,6 May be appropriate; 7,8,9 Usually appropriate		

Treatment options Treatment	Rating	Comments
ABVD × 2, then RT	3	Two cycles are inadequate in an unfavorable patient, as is the case here.
ABVD × 4, then RT	8	
ABVD × 6, then RT	4	Six cycles are probably too much but might be a consideration if there was a partial response by PET criteria after 4 cycles.
ABVD × 6, no RT	6	
Stanford V over 8 weeks, then RT	7	Stanford V is a well-described program with published results documenting its use in unfavorable patients.
Stanford V over 8 weeks, no RT	3	
BEACOPP × 2, ABVD × 2, then RT	6	This procedure is not widely used in the United States but is commonly used in Europe because of concerns of toxicity. The risk of ovarian failure is mitigated by the use of luteinizing hormone-releasing hormone agonists.
MOPP × 6, then RT	2	
ABVD/MOPP × 4–6, then RT	3	
ABVE-PC × 4, then RT only if slow or incomplete response	3	There is no experience with this pediatric regimen in adults.
Rating Scale: 1,2,3 Usually not appropriate; 4,5,6 May be appropriate; 7,8,9 Usually appropriate		

Note: Abbreviations used in the tables are listed at the end of the "Major Recommendations" field.

Variant 2: 26-year-old man with stage IB NSHL; supradiaphragmatic, bulky disease 10 cm in the neck; fevers >38ºC and drenching night sweats; complete resolution of FDG uptake on PET scan after 2 cycles (Deauville score 2); partial response by CT (>50% reduction) after 6 cycles of ABVD. Deauville score 2 after repeat PET scan at chemotherapy completion.

Treatment	Rating	Comments
Radiation field		
IFRT to neck	6	There is overlap between IFRT and ISRT. The precise definition of ISRT is in evolution. IFRT is not wrong, but ISRT is preferred.
ISRT to neck	8	
Mantle	2	
Subtotal nodal irradiation	1	
Radiation dose		
20 to <30 Gy	4	There are limited data to use lower doses from Duke, India, and pediatric experiences after 6 cycles of chemotherapy. In addition, GHSG HD11 did not strictly show that 20 Gy was inferior to 30 Gy.
30–32 Gy	8	
>32–36 Gy	5	
>36–40 Gy	3	
>40 Gy	2	
Rating Scale: 1,2,3 Usually not appropriate; 4,5,6 May be appropriate; 7,8,9 Usually appropriate		

Note: Abbreviations used in the tables are listed at the end of the "Major Recommendations" field.

Variant 3: 26-year-old man, CS IIA NSHL with bulky mediastinal mass (11 cm) and nonbulky bilateral neck disease; complete resolution of FDG uptake on PET scan after 2 cycles (Deauville score 2); partial response by CT (>50% reduction) after 4 cycles of ABVD.

Treatment	Rating	Comments
Additional chemotherapy	6	Bulky mediastinal adenopathy has been a criterion for advanced-stage disease in some studies in which 6 cycles of ABVD have been used and is considered more of a standard by some experts. The GHSG HD14 finding that more intensive chemotherapy is better is suggestive that more cycles of ABVD chemotherapy may be desirable as an alternative to the use of BEACOPP × 2 + ABVD × 2.
Radiation field (after chemotherapy)		
IFRT to mediastinum and bilateral neck	6	
ISRT to mediastinum and bilateral neck	9	
Mantle	2	
Subtotal nodal irradiation	1	
Radiation dose (after chemotherapy)		
20 to <30 Gy	3	
30–32 Gy	8	
>32–36 Gy	6	
>36–40 Gy	4	
20–21 Gy, then boost mediastinum dose to 30-32 Gy	5	Shrinking fields or differential dosing can be a good strategy to limit dose to the heart or lungs, especially if 6 cycles of ABVD are administered. Some limited data suggest bulky disease may be less well controlled with a lower dose, justifying this approach to improve the therapeutic ratio. Moreover, pediatric data suggest that using lower radiation doses appears to be effective in younger patients.
20–21 Gy, then boost mediastinum dose to 36-40 Gy	3	
Rating Scale: 1,2,3 Usually not appropriate; 4,5,6 May be appropriate; 7,8,9 Usually appropriate		

Note: Abbreviations used in the tables are listed at the end of the "Major Recommendations" field.

Variant 4: 26-year-old woman, CS IIB NSHL with bulky mediastinal (13 cm) and left supraclavicular disease; >75% reduction of mass by CT (3 cm residual after chemotherapy) and negative PET after both 2 and 6 cycles of ABVD chemotherapy (both Deauville scores 2).

Treatment	Rating	Comments
Radiation dose		
No further RT	5	This treatment may be appropriate but there was disagreement among panel members on the appropriateness rating as defined by the panel's median rating. Despite evidence that omission of RT for bulky Hodgkin lymphoma is detrimental to disease control, there was concern that the risk of side effects such as secondary breast cancers and cardiopulmonary problems might outweigh the benefits.
If RT given, radiation dose		
20 to <30 Gy	5	This treatment may be appropriate but there was disagreement among panel members on the appropriateness rating as defined by the panel's median rating. There was no agreement that doses <30 Gy may be appropriate after 6 cycles of ABVD in this instance.
30–32 Gy	8	
>32–36 Gy	5	
>36–40 Gy	3	
Rating Scale: 1,2,3 Usually not appropriate; 4,5,6 May be appropriate; 7,8,9 Usually appropriate		This dose has been used in recent trials but is generally felt to

Treatment	Rating	Comments
Boost mediastinum dose to 40 Gy	3	
Mediastinal volume		
Treat postchemotherapy volume only laterally	8	
Treat prechemotherapy volume laterally	3	
Inferior margin 1-2 cm below prechemotherapy volume	7	
Treat prechemotherapy volume to 15–20 GY, then shrink	4	
Inferior margin 1–2 cm below postchemotherapy volume	4	
Inferior margin 5 cm below post-chemotherapy volume	3	
Inferior margin approximately at diaphragm	3	
Inferior margin 5 cm below prechemotherapy volume	3	
Rating Scale: 1,2,3 Usually not appropriate; 4,5,6 May be appropriate; 7,8,9 Usually appropriate		

be too high.

Note: Abbreviations used in the tables are listed at the end of the "Major Recommendations" field.

Variant 5: 26-year-old woman, CS IIB NSHL with bulky mediastinal (13 cm) and left supraclavicular disease treated with ABVD × 6; >75% reduction of mass by CT after 2 cycles (3 cm residual mass after chemotherapy) with good PET response (Deauville score 3); but after 6 cycles of ABVD chemotherapy residual mass is stable on CT but PET response looks worse (Deauville score 4). A needle biopsy of mediastinal mass shows CD30+ Reed-Sternberg cells.

Treatment	Rating	Comments
RT alone	4	
If RT given alone, radiation dose should be:		
30–32 Gy	3	
>32–36 G	4	
>36–40 Gy	5	
30–32 Gy, boost mediastinum to 36 Gy	5	This treatment may be appropriate but there was disagreement among panel members on the appropriateness rating as defined by the panel's median rating.
30-32 Gy, boost mediastinum to 40 Gy	7	
If RT given alone, radiation volume should be:		
Mediastinal site only	5	
Left neck and mediastinum	7	
Mantle field	3	
Extended field (subtotal nodal or total nodal)	2	
Salvage chemotherapy alone	4	
Salvage chemotherapy followed by consolidative RT	6	
If consolidative RT given, radiation dose should be:		
30-32 Gy	5	

Treatment	Rating	Comments
>32-36 Gy	6	
>36-40 Gy	6	
30-32 Gy, boost mediastinum to 36 Gy	7	
30-32 Gy, boost mediastinum to 40 Gy	6	
If consolidative RT given, radiation volume should be:		
Mediastinal site only	5	
Left neck and mediastinum	8	
Mantle field	4	
Extended field (subtotal nodal or total nodal)	2	
Salvage chemotherapy with auto–stem cell transplantation (auto-SCT)	6	
Salvage chemotherapy with auto-SCT, followed by consolidative RT	8	
If consolidative RT given, radiation dose should be:		
30-32 Gy	6	
>32-36 Gy	6	
>36-40 Gy	5	
30-32 Gy, boost mediastinum to 36 Gy	5	This treatment may be appropriate but there was disagreement among panel members on the appropriateness rating as defined by the panel's median rating.
30-32 Gy, boost mediastinum to 40 Gy	5	This treatment may be appropriate but there was disagreement among panel members on the appropriateness rating as defined by the panel's median rating.
If consolidative RT given, radiation volume should be:		
Mediastinal site only	5	This treatment may be appropriate but there was disagreement among panel members on the appropriateness rating as defined by the panel's median rating.
Left neck and mediastinum	8	
Mantle field	3	
Extended field (subtotal nodal or total nodal)	2	
Rating Scale: 1,2,3 Usually not appropriate; 4,5,6 May be appropriate; 7,8,9 Usually appropriate		

Note: Abbreviations used in the tables are listed at the end of the "Major Recommendations" field.

Summary of Literature Review

Historical Overview

A brief historical view of the management of Hodgkin lymphoma is necessary to place current management concepts and treatment controversies in proper context. Early in the empiric development of radiation oncology many decades ago, Hodgkin lymphoma was found to ostensibly spread to contiguous lymph node sites in its natural history and to be very radiation sensitive. The use of extended-field radiation therapy (EFRT) (to encompass grossly evident lymphoma and adjacent microscopic disease) and appropriate radiation dosing led to the first cures of this disease. With the development of megavoltage radiation therapy (RT) and with improved staging of Hodgkin lymphoma by staging laparotomy, cure rates for early-stage Hodgkin lymphoma steadily improved. Patients with more advanced stages and relapses were found to benefit from the introduction of multiagent chemotherapy. MOPP (mechlorethamine, vincristine, procarbazine, and prednisone) and its variants constituted the first generation of successful therapy, although ABVD (adriamycin, bleomycin, vinblastine, and dacarbazine) and its variants have been a second generation having improved efficacy and toxicity profiles. With identification of risk factors for relapse, chemotherapy was often added to subtotal or total nodal irradiation for patients deemed to have unfavorable early-stage Hodgkin lymphoma. Although there were early theoretical

considerations that radiation dose and volumes could be reduced when effective chemotherapy was given, decades of clinical trials have led to current standards of care using combined-modality therapy (CMT) for stage I and II Hodgkin lymphoma in which radiation doses and fields have been substantially reduced to minimize toxicity while maintaining high cure rates. Radiation techniques are still in evolution while there are ongoing efforts to see which patients can be treated with chemotherapy alone.

Driving the current debates on optimizing therapy of Hodgkin lymphoma has been the desire to minimize the risk of secondary malignant neoplasms (SMN) and cardiovascular effects of therapy. With highly successful cure rates of Hodgkin lymphoma, these long-term toxicities of therapy seen over many years and decades of follow-up have provided an impetus for risk-adapted combined chemotherapy and reduced-intensity RT. Moreover, modern imaging with computed tomography (CT) scanning, positron emission tomography (PET) imaging (which has supplanted the use of Gallium scanning), and, to a lesser degree, magnetic resonance imaging (MRI) has eliminated the need for staging laparotomy. In the modern diagnostic workup after a pathologic diagnosis using modern immunohistochemistry, PET/CT scanning has become increasingly standard, along with selected biopsy of bone marrow and other disease sites only when results would change therapy.

Definition of Early-stage Unfavorable Hodgkin Lymphoma

In addition to staging, the identification of prognostic factors has taken on importance as a determinant of treatment algorithms. Complicating this matter are 3 concepts. First, prognostic factors are in flux as more effective or higher-intensity therapy may negate adverse risk factors previously demonstrated. Second, various risk-stratification schemes have been used by different institutions and cooperative groups to allocate patients to various treatment regimens, making comparisons of patient populations challenging. Thus, there is some variability in classification of Hodgkin patients into favorable and unfavorable groupings. Lastly, there is an evolving understanding that early response to systemic therapy may be an important prognostic factor that can be used to guide further treatment decisions. Although this concept is under investigation in adults with Hodgkin lymphoma, one may acknowledge that response-based therapy has recently developed firm roots in pediatric Hodgkin lymphoma treatment paradigms.

Dating from the time that early-stage Hodgkin lymphoma was treated with subtotal or total nodal irradiation including splenic irradiation, often termed EFRT, numerous adverse prognostic factors in stage I–II disease have identified those patients who benefit from CMT. As a result, the concept of risk-adapted therapy, in which the presence of poor prognostic factors drives more intensive therapy, has been developed; at the same time, favorable factors identify a population appropriately treated with less intensive therapy designed to maintain high cure rates with fewer acute and late side effects. Prognostic factors identified in these analyses include the number of involved lymphoid regions, the size of individual nodes, the extent of mediastinal disease, patient gender and age, the presence of B symptoms or pruritus, histology, erythrocyte sedimentation rate (ESR), and overall tumor burden, as measured by number of sites and disease bulk.

There has been general consensus that 2 of these factors in stage I–II Hodgkin lymphomas should most influence management decisions. The first is constitutional B symptoms: unexplained fevers >38°C, drenching night sweats, or significant weight loss >10% in 6 months, as clearly defined in the Ann Arbor staging classification system. The presence of B symptoms is correlated with a higher likelihood of systemic disease, including occult subdiaphragmatic disease when staging laparotomies were once performed. Evidence suggests that fevers and weight loss have more prognostic significance than night sweats alone.

The second prognostic factor that should influence treatment selection is the presence of large mediastinal adenopathy or bulky disease in nonmediastinal sites. A variety of definitions of large mediastinal adenopathy have been reported in the literature. The most commonly used definition is based on measurement of the maximum width of the mediastinal mass on a standing posteroanterior chest radiograph, compared with the maximum intrathoracic diameter. A ratio greater than 1:3 is defined as "bulky." Other reports have used a ratio with the intrathoracic width at T5–6 as the denominator, and still others use absolute measurements, surface area calculations, or volume measurements. Bulky disease in nonmediastinal sites has similarly been classified by varying definitions. Some protocols define bulky as ≥10 cm, and others use ≥5 cm or ≥6 cm.

In interpreting results of trials, it is important to note that the definition of unfavorable-prognosis, early-stage disease varies among cooperative groups. The European Organization for Research and Treatment of Cancer (EORTC) and Groupe d'Etudes des Lymphomes de l'Adulte (GELA) specify the following as unfavorable factors: age >50 years, ESR ≥50 in the absence of B symptoms, ESR ≥30 with B symptoms, ≥4 sites of involvement, or bulky mediastinal involvement. For the German Hodgkin Lymphoma Study Group (GHSG), the following are considered unfavorable factors: ESR ≥50 in the absence of B symptoms, ESR ≥30 with B symptoms, ≥3 sites of involvement, extranodal involvement, or a bulky mediastinal mass. Many of the North American cooperative groups, however, have classified stage I and II patients with either bulky disease or B symptoms under the rubric of advanced-stage disease for purposes of protocol eligibility, despite the potential for overtreatment. For instance, stage I/II patients with bulky mediastinal adenopathy accounted for a third of patients in the Eastern Cooperative Oncology Group (ECOG) E2496 Intergroup trial of locally extensive and advanced Hodgkin lymphoma. Table 2 in the original guideline document summarizes some of these prognostic groupings. There is also an ongoing research effort to identify biologically based prognostic factors. The density of macrophages as measured by CD68-positive infiltrating cells was found to be one such prognostic factor by one group of investigators. Within the context of the E2496 study, this finding was confirmed, but a 23-gene expression panel proved to be a better determinant of prognosis. Recent

pediatric experience within the Children's Oncology Group has led to a simplified prognostic score based on just 4 factors (stage IV, large mediastinal mass, fever, and albumin level).

Treatment Principles

The understanding that an unacceptably high rate of late complications stems from external beam RT has led to the abandonment of primary RT. Although cardiovascular complications from mediastinal RT increase as a function of radiation dose and volume, anthracyclines also cause heart disease—both cardiomyopathy with age-dependent thresholds and by potentiating the effects of RT on risk of congestive heart failure, coronary artery disease, and valvular heart disease. However, the chief impetus to changing treatment philosophies has been the risk of SMN. Although beyond the scope of this brief review, the risk of secondary malignancies is dependent on patient age, gender, and specifics of treatment exposure to normal tissues. Conceptions that alkylating agents independently cause leukemias and that RT causes solid tumors are overly simplistic and probably inaccurate.

Nevertheless, CMT consisting of chemotherapy followed by lower-dose RT represents the standard of care for most patients with unfavorable stage I–II Hodgkin lymphoma. Anthracycline-containing regimens are the most widely accepted systemic therapy as part of CMT, with ABVD being the prototype. Various hybrid regimens, such as MOPP/ABV, have been used. Stanford V, a 12-week, 7-drug regimen that is administered on a weekly basis, includes the topoisomerase II inhibitor etoposide but contains lower cumulative doses of mechlorethamine, adriamycin, and bleomycin than do MOPP and ABVD, respectively. BEACOPP (bleomycin, etoposide, adriamycin, cyclophosphamide, vincristine, procarbazine, and prednisone) is another active and efficacious regimen developed by the GHSG originally for advanced-stage Hodgkin lymphoma.

In most trials of CMT, RT has evolved from EFRT to involved-field radiation therapy (IFRT) directed at all regions of initial involvement at diagnosis. The definition of IFRT has been detailed elsewhere. In a continuous effort to limit the toxicity of radiation in the presence of effective chemotherapy, involved-site radiation therapy (ISRT) has been introduced as the new standard of care. The International Lymphoma Radiation Oncology Group (ILROG) recently published the guidelines of ISRT. The main differences compared to IFRT are 1) use of the modern definition of treatment volume as defined by the International Commission on Radiation Units and Measurements Report and 2) the extended fields in IFRT are now replaced by limited volumes based solely on detectable disease at presentation using contrast-enhanced CT and PET/CT. Suffice it to say, following chemotherapy, lymphatic regions initially involved at diagnosis are targeted. The superior-inferior extent of the radiation field typically encompasses the prechemotherapy extent of disease, although the lateral or radial extent can be limited to the postchemotherapy extent of disease in the mediastinum. The initial lateral extent of mediastinal disease should not be treated unless there is known extranodal disease extension into bone or chest wall. The dose fractionation is variable from one trial to another, but dose per fraction has varied from 1.5 to 2.0 Gy; whether or not there are any significant radiobiological differences in this fractional dose range is unclear. Also unclear is the use of shrinking field technique, where bulky or slowly responding disease is differentially dosed higher than other areas. Often, simple anterior-posterior fields have been used. Limiting excess radiation to critical structures in the vicinity of involved sites is essential in today's radiation treatment. Technical advances represented by computer planning have been introduced, as represented by the use of intensity-modulated radiation therapy (IMRT), breath-hold techniques, image-guided therapy, and 4-dimensional (4-D) CT treatment planning. Along the same lines, proton beam RT is sometimes an appropriate consideration.

See the original guideline document for discussion of important clinical trials.

Involved-site Radiation Therapy

In recent years, there has been growing interest in further limiting the radiation treatment volume to involved-node radiation therapy (INRT). The definition of INRT varies from group to group. In the EORTC/GELA H11 trial for early-stage, unfavorable-prognosis Hodgkin lymphoma (discussed below), INRT was adopted in both the standard and experimental arms. The GHSG is enrolling patients with unfavorable-prognosis, early-stage disease in a randomized trial (HD17) comparing IFRT versus INRT. Results of these trials, including details on patterns of failure, will clarify the role of INRT in early-stage patients. Recently, a new set of field designs, the ISRT, have been developed and endorsed by the steering committee of ILROG. Led by experienced radiation oncologists specializing in lymphoma who initially organized the standardization of IFRT fields in the 2-D era a decade ago, the ISRT fields are a "modernized" version of IFRT. These new field designs were developed to take into consideration modern technology, including the use of staging PET/CT scans, 3-D and 4-D treatment planning with CT scanners, conformal treatment techniques, and the use of image guidance, to replace the antiquated IFRT that was based on 2-D treatment planning and bony anatomy. These treatment volumes are expected to be somewhat smaller than the traditional IFRT but larger than INRT for patients who do not have adequate imaging necessary for INRT treatment planning. A detailed description of the ISRT concept has been published and has been recommended in the 2013 National Comprehensive Cancer Network guidelines for Hodgkin lymphoma.

The appropriate radiation dose in patients with unfavorable-prognosis, early-stage disease after chemotherapy was addressed by the GHSG HD11 trial described above. After 4 cycles of BEACOPP, a significant difference in 5-year FFTF between 20 Gy and 30 Gy was not observed. However, after 4 cycles of ABVD, an inferiority of the 20-Gy arm could not be excluded, with a 4.7% lower absolute difference in 5-year FFTF

in the 20-Gy arm not reaching the 7% threshold margin in the trial design. This led to the conclusion that a reduction of radiation dose from 30 Gy to 20 Gy of IFRT in unfavorable-prognosis patients may be justified after BEACOPP but not clearly after ABVD when 4 cycles of chemotherapy are administered. At present, there is no reported subgroup analysis of patients from the GHSG HD11 or HD14 trials of bulky mediastinal adenopathy to compare to the results from the E2496. Consequently, there is a range of chemotherapy cycles and radiation doses that are deemed acceptable but may have significantly different late effects. Additional follow-up data will be required for further elucidation. In addition, retrospective data from Duke, Yale, and Tata Memorial Hospital in India suggest that after 4–6 cycles of anthracycline-based chemotherapy with a complete response at chemotherapy completion (emphasizing 6 cycles for bulky disease), radiation doses in the 20 Gy to 25 Gy range may yield good results (see Variant 2 and Variant 3 above).

Response-based Treatment Paradigm

PET has emerged as a useful tool in the staging and follow-up of patients with Hodgkin lymphoma. Additionally, PET response of chemotherapy has been shown to be a powerful prognostic factor. There is an increasing interest to see if response to chemotherapy by PET assessment will help select patients who may not benefit from RT. A recent randomized trial evaluated whether RT can be omitted in patients with bulky masses at diagnosis who show a complete response by PET following chemotherapy. One hundred sixty patients who had a complete response to induction chemotherapy with 6 cycles of VEBEP (vinblastine, etoposide, bleomycin, epirubicin, and prednisone), but with a residual mass and a PET-negative scan, were randomized to undergo either observation or consolidative RT to 32 Gy in 20 fractions. The EFS rate was significantly lower in the observation arm than in the RT arm (86% versus 96%, P=0.03).

Whether an early response to chemotherapy as judged by PET imaging after the initial 2 cycles of chemotherapy might better distinguish which patients require RT is being tested in several clinical trials. The Children's Oncology Group has completed a large trial (COG AHOD0031) in "intermediate-risk" patients, defined as stage I–II with either bulk or extranodal involvement through stage IIIA–IVA without bulk, in which rapidly responding patients treated with ABVE-PC (adriamycin, bleomycin, vincristine, etoposide, cyclophosphamide, and prednisone) were randomized to chemotherapy alone for total of 4 cycles versus the same chemotherapy with IFRT to 21 Gy in 14 fractions. Results show a nonstatistical difference in 4-year DFS of 87.9% (95% CI, 83.7%–91.1%) for patients randomized to receive IFRT versus 84.3% (95% CI, 79.8%–87.9%) for those randomized to no IFRT (P=0.11).

The ongoing EORTC/GELA H10U trial also explored the use of PET response to identify patients with unfavorable-prognosis, early-stage disease in whom RT can be omitted. The standard arm of this trial consisted of 4 cycles of ABVD followed by INRT to 30 Gy, although patients on the experimental arm received 2 cycles of ABVD followed by a PET scan. If the scan was negative, patients received 4 additional cycles of ABVD and then no further treatment. If the PET scan was positive, patients received 2 cycles of BEACOPPesc, followed by INRT to 30 Gy. Interim results published show an excess of relapses in the patients who had INRT omitted. Stopping rules resulted in this experimental arm of this trial to be closed. Thus, on this EORTC/GELA H10U trial, patients with a rapid early response are still getting INRT. Several other trials are testing the concept that early response assessed by PET scan will be a predictor of who can avoid RT if abnormal fluorine-18-2-fluoro-2-deoxy-D-glucose (FDG) uptake has completely resolved after cycle 2. Conversely if PET after cycle 2 is positive, augmentation of chemotherapy is being tested. Thus for the time being, in adults with early-stage Hodgkin lymphoma there is insufficient evidence to support the omission of RT based on PET response or early PET response; such an approach should be pursued in the context of a clinical trial (see Variant 4 above).

An international consensus panel has evaluated the growing evidence using PET/CT imaging to grade response to systemic therapy and now recommends the use of a visual analog score for interim and end-of-therapy assessments using the 5-point Deauville scale (see Table 1 in the original guideline document). This 5-point scale uses the FDG uptake of the mediastinal blood pool and the liver for comparison. A score of 1 or 2 (in midtherapy or end-of-therapy PET/CT) is considered to represent a complete response, and a score of 3 is considered to predict a favorable outcome. However, a score of 4 or 5 at the end of therapy is considered to be treatment failure; these patients should be considered for a biopsy to confirm the presence of residual disease before salvage therapy.

Management of Refractory Hodgkin Lymphoma

Recurrence or persistence of disease occurs in approximately 10% to 15% of early-stage patients, although it is higher in advanced-stage patients, approaching 30% to 40%. Although precise data are difficult to find, perhaps a third of this category of poor-prognosis patients includes high-risk primary refractory disease. In the GHSG, 3807 patients with intermediate or advanced Hodgkin lymphoma enrolled in their various trials from 1988 to 1998. Of these, 239 patients (6.3%) were found to have primary refractory disease. With the clinical adoption of PET/CT imaging to assess chemotherapy response, primary refractoriness may have a higher incidence and is currently defined either by progression at any time during chemotherapy or RT and up to 3 months after the end of treatment, and/or by persistence of a PET-positive residual mass. Thus, a Deauville score of 4 or 5 at the completion of chemotherapy defines refractory disease, but only if correlated with an enlarged mass or node on CT scanning (to mitigate the problem of false-positive scans) (see Variant 5 above).

Data on the optimal management of this situation are complex, particularly as the literature has lumped refractory lymphoma with relapsed disease.

Some studies of hematopoietic stem cell transplantation even combine Hodgkin and non-Hodgkin patients. There are no good comparisons of different salvage regimens for refractory Hodgkin lymphoma, such that individual judgment is required. Some dogma exists that chemotherapy failures cannot be managed with RT. However, limited sites of persistent disease can anecdotally be controlled with RT to 30 Gy to 45 Gy. In the pre-PET era within the GHSG experience, a subset of 47 patients with primary refractory Hodgkin lymphoma with limited sites of disease were able to be managed with salvage RT with curative intent using a broad mix of radiation treatment volumes from total nodal to involved fields. With a median radiation dose of 40 Gy, the complete response rate was 62%, although the 4-year actuarial freedom from second relapse rate was a disappointing 22%. Nevertheless, a renewed interest and basis for RT to manage limited refractory disease now derives from the GHSG HD15 trial for advanced disease. In the context of aggressive backbone systemic therapy with BEACOPPesc × 6, consolidative RT to sites of persistent PET activity for 30 Gy contributed to an excellent DFS. With 11% of enrolled patients requiring consolidative RT, the 5-year FFTF was 89.4%. How this might translate to earlier-stage patients receiving less intensive systemic therapy needs further study.

Alternatively, there is extensive experience with second-line systemic therapy for refractory disease using platinum-containing regimens such as DHAP (dexamethasone, high-dose cytarabine [Ara-C], and cisplatin) or ICE (ifosfamide, carboplatin, and etoposide). These and other second-line combinations have not been compared directly in a randomized trial. Choice is based on side effects, experience, and expert consensus. Remission rates are in the 30% to 40% range, as reviewed by a group of researchers. After adequate cytoreduction, autologous stem cell harvesting can be performed to facilitate high-dose chemotherapy and autologous hematopoietic stem cell transplantation. BEAM (carmustine [BCNU], etoposide, cytarabine, and melphalan) and CBV (cyclophosphamide, carmustine, and etoposide) are common regimens prior to an autotransplant. Patients who are able to undergo this therapeutic sequence have 8- to 10-year OS rates of 21% to 27%, with FFTF on the order of 16%. However, if patients are PET negative going into an autotransplant, results are improved. One study showed that progression-free survival of the PET-negative group of lymphoma patients after conventional-dose chemotherapy followed by high-dose chemotherapy salvage was 72% versus 23% for the PET-positive group. Primary refractory disease has been generally categorized as high risk relative to patients relapsing >12 months after first remission; as such, some investigators have concluded that such patients may be best treated with a tandem transplant. A multicenter European transplant trial for Hodgkin lymphoma, for instance, showed that poor-risk patients, including those with primary refractory disease, had a 5-year freedom from second failure and OS of 46% and 57%, respectively, using a tandem autotransplant. The first transplant used BEAM or CBV, and the second transplant was either TBI (total body irradiation) and melphalan or busulfan-melphalan, depending on prior RT exposures. TBI-based treatment was favored when feasible and used 12 Gy in 6 fractions over 3 days. Concerns regarding the toxicity of TBI have led some investigators to incorporate total or subtotal lymphoid irradiation into some autotransplant regimens instead of TBI, especially when there is a nodal pattern of failure for a given patient. Needless to say, for early-stage patients with refractory disease this form of tandem transplant may seem to be excessive therapy as second-line treatment by some experts.

The recent development of new agents such as brentuximab vedotin (an anti-CD30 antibody conjugated with a microtubule toxin) in phase II trials shows durably good response rates over historical experience with third-line cytotoxic chemotherapy in patients recurring after an autotransplant. Brentuximab is now under investigation as first- and second-line therapy in combination with chemotherapy (albeit with the avoidance of bleomycin to avoid undue risk for pneumonitis).

For patients who complete salvage chemotherapy with a good response, which may often include high-dose chemotherapy with autotransplantation, there may be consideration of consolidation RT to sites of resistant disease. Several retrospective studies suggest an improvement in progression-free survival from such RT. A group at Emory performed a matched case-control study and showed a significant improvement in DFS with RT in this setting, but not OS. Even so, sites of initial bulky disease that remain resistant or sluggish to respond to chemotherapy were associated with sites of additional recurrence despite application of consolidation RT. Investigators from Chicago reported that IFRT reduced local relapse rates in sites of prior Hodgkin involvement from 43% to 26%, thus improving 5-year local control rates in all sites, nodal sites, and sites that were resistant to high-dose chemotherapy. Another group at Stanford reported only 4 local failures out of 67 irradiated sites. Moderate-dose RT as part of salvage therapy is commonly practiced, although radiation treatment volumes need to be highly individualized to balance toxicity and disease-control concerns. Whether all sites of initial involvement at diagnosis need to be irradiated in this scenario is not well understood or worked out. Too small a treatment volume may defeat the benefit to RT. Timing of consolidative RT is controversial. Some concern exists for chest RT prior to autotransplant having an undue risk of pneumonitis, as initially reported by a Toronto group. Other investigators, such as at Memorial Sloan Kettering Cancer Center, dispute this and prefer to give RT prior to high-dose therapy and transplant. The recommended radiation dose is at least 30 Gy with a potential boost of 6 Gy to 10 Gy, particularly for sites of disease not in metabolic complete response on PET imaging prior to transplant.

Summary of Recommendations

Core Concept

- The standard of care for unfavorable stage I–II Hodgkin lymphoma is CMT, consisting of chemotherapy followed by low dose RT (generally 30 Gy, but certain circumstances justify lower doses).

Chemotherapy

- The most widely accepted chemotherapy regimen is ABVD.
- ABVD × 4–6, BEACOPP × 2 + ABVD × 2 ("2 + 2"), Stanford V, or ABVE-PC (pediatric regimen) are well documented, with variable radiation dose prescriptions and volumes based on specific regimens and responses to chemotherapy.

Radiation Dose, Volume, and Techniques

- A range of radiation dose from 20 Gy to 30 Gy is acceptable when there is a good response to initial chemotherapy. For patients meeting multiple criteria for unfavorable risk and receiving 4 cycles of chemotherapy, such as ABVD or BEACOPP × 2 + ABVD × 2, 30 Gy is strongly recommended. Some situations may justify doses <30 Gy, particularly when there is a strong rationale to reduce toxicity attributable to RT. This can be considered when there is a good response to 6 cycles of ABVD or similar chemotherapy, although this point requires further study. Patients who are young adults following pediatric-styled chemotherapy regimens can receive 20 Gy to 25 Gy. Moreover, patients who have nonbulky disease and 3 sites of involvement may be considered either favorable or unfavorable under different criteria and may well have an improved therapeutic ratio with doses below 30 Gy.
- A dose per fraction in the range of 1.5 Gy to 2.0 Gy is acceptable.
- Specific combined modality regimens have been well studied. For instance, the GHSG in particular has a well-described set of definitions for favorable versus unfavorable early-stage disease based on favorable patients having none of the following factors: >2 sites of disease, ESR ≥50 mm/h without B symptoms, ESR ≥30 mm/h in the presence of B symptoms, no bulky mediastinal disease, and no extranodal disease. In unfavorable patients with at least 1 risk factor, 4 cycles of chemotherapy and 30 Gy in 15 to 17 fractions have optimal results. However, other chemotherapy regimens of differing intensity and number of cycles may allow for lower radiation doses to reduce late effects.
- Higher radiation doses >30 Gy should be reserved for patients who have poor response to chemotherapy. The concept of using 36 Gy for bulky-disease consolidation in all patients is no longer reasonable as the risks for secondary malignancies and cardiovascular disease are well described.
- Anterior-posterior fields are often simple and efficacious. However, more conformal techniques using multiple fields, IMRT, volumetric modulated arc therapy, and proton RT may be useful to limit toxicities. Specific newer radiation techniques are beyond the scope of this review, but suffice it to say that 4-D treatment planning and deep inspiration breath-hold techniques are under investigation. Inherent with these techniques, the modern concept of ISRT is recommended; margins of RT are expected to be smaller as part of volumetric 3-D treatment planning rather than the historic anatomic field definitions of IFRT.
- Differential dosing or a shrinking field technique to account for a variable burden of disease based on bulk at presentation or in response to chemotherapy is a reasonable method to balance toxicity and efficacy.

Chemotherapy Alone

- Use of chemotherapy alone, such as 6 cycles of ABVD, is an acceptable option in selected patients, particularly in those without bulky disease at diagnosis, as this reduces the risk of late effects, especially when higher-dose RT is applied as adjuvant therapy. However, lower-dose radiation in the 21 Gy to 25 Gy range is acceptable after ABVD × 6 when late toxicity concerns are deemed to be minimal, as low-dose RT may help prevent a relapse.
- If the decision to use ABVD × 6 alone is based on early response to chemotherapy, caution is advised until the results of the EORTC/GELA H10U and other trials are mature and published.
- The pediatric regimen ABVE-PC can be used in pediatric, adolescent, and young adult patients without RT when there is a rapid early response after 2 cycles, especially if defined by a negative PET scan and if at the end of chemotherapy there is a complete response by CT criteria.

Abbreviations

- ABVD, adriamycin, bleomycin, vinblastine, and dacarbazine
- ABVE-PC, adriamycin, bleomycin, vincristine, etoposide, cyclophosphamide, and prednisone
- BEACOPP, bleomycin, etoposide, adriamycin, cyclophosphamide, vincristine, procarbazine, and prednisone
- C, Celsius
- CS, clinical stage
- CT, computed tomography
- ECOG, Eastern Cooperative Oncology Group (the National Cancer Institute of Canada)
- ESR, erythrocyte sedimentation rate
- FDG, fluorine-18-2-fluoro-2-deoxy-D-glucose

- GHSG, German Hodgkin Lymphoma Study Group
- IFRT, involved-field radiation therapy
- ISRT, involved-site radiation therapy
- MOPP, mechlorethamine, vincristine, procarbazine, and prednisone
- PET, positron emission tomography
- RT, radiation therapy

Clinical Algorithm(s)

Algorithms were not developed from criteria guidelines.

Scope

Disease/Condition(s)

Hodgkin lymphoma – unfavorable clinical stage I and II

Guideline Category

Treatment

Clinical Specialty

Family Practice

Internal Medicine

Oncology

Radiation Oncology

Radiology

Intended Users

Advanced Practice Nurses

Health Plans

Hospitals

Managed Care Organizations

Physician Assistants

Physicians

Students

Utilization Management

Guideline Objective(s)

To evaluate the appropriateness of treatment procedures for patients with unfavorable clinical stage I and II Hodgkin lymphoma

Target Population

Patients with unfavorable clinical stage I and II Hodgkin lymphoma

Interventions and Practices Considered

1. Overall plan
    - Combined modality therapy
    - Chemotherapy alone
    - Radiation therapy (RT) alone
    - No further RT
2. Radiation field
    - Involved-field radiation therapy (IFRT) to neck
    - IFRT to mediastinum and bilateral neck
    - Involved-site radiation therapy (ISRT) to neck
    - ISRT to mediastinum and bilateral neck
    - Subtotal nodal irradiation
    - Mantle
3. Chemotherapy treatment options
    - Adriamycin, bleomycin, vinblastine, and dacarbazine (ABVD)
    - Bleomycin, etoposide, doxorubicin, cyclophosphamide, vincristine, procarbazine, and prednisone (BEACOPP)
    - Stanford V
    - Mechlorethamine, vincristine, procarbazine, and prednisone (MOPP)
    - Adriamycin, bleomycin, vincristine, etoposide, cyclophosphamide, and prednisone (ABVE-PC)
4. Duration of chemotherapy
5. Radiation dose
6. Radiation volume
7. Mediastinal volume
8. Salvage chemotherapy alone
9. Salvage chemotherapy followed by consolidative RT
10. Salvage chemotherapy with auto–stem cell transplantation (auto-SCT)
11. Salvage chemotherapy with auto-SCT, followed by consolidative RT

Major Outcomes Considered

- Utility of positron emission tomography (PET)
- Impact of prognostic factors
- Event-free survival rate (freedom from disease progression, freedom from treatment failure)
- Overall survival rate
- Complete response/remission rate
- Secondary malignancy rates
- Treatment-related toxicity
- Death rate

Methodology

Methods Used to Collect/Select the Evidence

Hand-searches of Published Literature (Primary Sources)

Hand-searches of Published Literature (Secondary Sources)

Searches of Electronic Databases

Description of Methods Used to Collect/Select the Evidence

Literature Search Summary

Of the 24 citations in the original bibliography, 22 were retained in the final document. Articles were removed from the original bibliography if they were more than 10 years old and did not contribute to the evidence or they were no longer cited in the revised narrative text.

A new literature search was conducted in June 2015 to identify additional evidence published since the *ACR Appropriateness Criteria® Hodgkin Lymphoma-Unfavorable Clinical Stage I and II* topic was finalized. Using the search strategy described in the literature search companion (see the "Availability of Companion Documents" field), 66 articles were found. Three articles were added to the bibliography. Sixty-three articles were not used due to either poor study design, the articles were not relevant or generalizable to the topic, the results were unclear, misinterpreted, or biased, or the articles were already cited in the original bibliography.

The author added 58 citations from bibliographies, Web sites, or books that were not found in the new literature search.

See also the American College of Radiology (ACR) Appropriateness Criteria® literature search process document (see the "Availability of Companion Documents" field) for further information.

Number of Source Documents

Of the 24 citations in the original bibliography, 22 were retained in the final document. The new literature search conducted in June 2015 identified three articles that were added to the bibliography. The author added 58 citations from bibliographies, Web sites, or books that were not found in the new literature search.

Methods Used to Assess the Quality and Strength of the Evidence

Weighting According to a Rating Scheme (Scheme Given)

Rating Scheme for the Strength of the Evidence

Definitions of Study Quality Categories

Category 1 - The study is well-designed and accounts for common biases.

Category 2 - The study is moderately well-designed and accounts for most common biases.

Category 3 - The study has important study design limitations.

Category 4 - The study or source is not useful as primary evidence. The article may not be a clinical study, the study design is invalid, or conclusions are based on expert consensus.

> The study does not meet the criteria for or is not a hypothesis-based clinical study (e.g., a book chapter or case report or case series description);
>
> *Or*
>
> The study may synthesize and draw conclusions about several studies such as a literature review article or book chapter but is not primary evidence;
>
> *Or*
>
> The study is an expert opinion or consensus document.

Category M - Meta-analysis studies are not rated for study quality using the study element method because the method is designed to evaluate individual studies only. An "M" for the study quality will indicate that the study quality has not been evaluated for the meta-analysis study.

Methods Used to Analyze the Evidence

Review of Published Meta-Analyses

Systematic Review with Evidence Tables

Description of the Methods Used to Analyze the Evidence

The topic author assesses the literature then drafts or revises the narrative summarizing the evidence found in the literature. American College of Radiology (ACR) staff drafts an evidence table based on the analysis of the selected literature. These tables rate the study quality for each article included in the narrative.

The expert panel reviews the narrative, evidence table and the supporting literature for each of the topic-variant combinations and assigns an appropriateness rating for each procedure listed in the variant table(s). Each individual panel member assigns a rating based on his/her interpretation of the available evidence.

More information about the evidence table development process can be found in the ACR Appropriateness Criteria® Evidence Table Development document (see the "Availability of Companion Documents" field).

Methods Used to Formulate the Recommendations

Expert Consensus (Delphi)

Description of Methods Used to Formulate the Recommendations

Rating Appropriateness

The American College of Radiology (ACR) Appropriateness Criteria (AC) methodology is based on the RAND/UCLA Appropriateness Method. The appropriateness ratings for each of the procedures or treatments included in the AC topics are determined using a modified Delphi method. An initial survey is conducted to elicit each panelist's expert interpretation of the evidence, based on the available data, regarding the appropriateness of an imaging or therapeutic procedure for a specific clinical scenario. The expert panel members review the evidence presented and assess the risks or harms of doing the procedure balanced with the benefits of performing the procedure. The direct or indirect costs of a procedure are not considered as a risk or harm when determining appropriateness (additional assumptions regarding rating appropriateness can be found in the document Rating Round Information). When the evidence for a specific topic and variant is uncertain or incomplete, expert opinion may supplement the available evidence or may be the sole source for assessing the appropriateness.

The appropriateness is represented on an ordinal scale that uses integers from 1 to 9 grouped into three categories: 1, 2, or 3 are in the category "usually not appropriate" where the harms of doing the procedure outweigh the benefits; and 7, 8, or 9 are in the category "usually appropriate" where the benefits of doing a procedure outweigh the harms or risks. The middle category, designated "may be appropriate," is represented by 4, 5, or 6 on the scale. The middle category is when the risks and benefits are equivocal or unclear, the dispersion of the individual ratings from the group median rating is too large (i.e., disagreement), the evidence is contradictory or unclear, or there are special circumstances or subpopulations which could influence the risks or benefits that are embedded in the variant.

The ratings assigned by each panel member are presented in a table displaying the frequency distribution of the ratings without identifying which members provided any particular rating. To determine the panel's recommendation, the rating category that contains the median group rating without disagreement is selected. This may be determined after either the first or second rating round. If there is disagreement after the first rating round, a conference call is scheduled to discuss the evidence and, if needed, clarify the variant or procedure description. If there is still disagreement after the second rating round, the recommendation is "may be appropriate."

This modified Delphi method enables each panelist to articulate his or her individual interpretations of the evidence or expert opinion without excessive influence from fellow panelists in a simple, standardized, and economical process. For additional information on the ratings process see

the Rating Round Information document.

Additional methodology documents, including a more detailed explanation of the complete topic development process and all ACR AC topics can be found on the ACR Web site (see also the "Availability of Companion Documents" field).

Rating Scheme for the Strength of the Recommendations

Not applicable

Cost Analysis

A formal cost analysis was not performed and published cost analyses were not reviewed.

Method of Guideline Validation

Internal Peer Review

Description of Method of Guideline Validation

Criteria developed by the Expert Panels are reviewed by the American College of Radiology (ACR) Committee on Appropriateness Criteria (AC).

Evidence Supporting the Recommendations

Type of Evidence Supporting the Recommendations

The recommendations are based on analysis of the current medical evidence literature and the application of the RAND/UCLA appropriateness method and expert panel consensus.

Summary of Evidence

Of the 83 references cited in the *ACR Appropriateness Criteria® Hodgkin Lymphoma-Unfavorable Clinical Stage I and II* document, 73 are categorized as therapeutic references including 33 well designed studies and 23 good quality studies. Additionally, 10 references are categorized as diagnostic references including 5 well designed studies, 1 good quality study, and 2 quality studies that may have design limitations. There are 19 references that may not be useful as primary evidence.

While there are references that report on studies with design limitations, 62 well designed or good quality study provides good evidence.

Benefits/Harms of Implementing the Guideline Recommendations

Potential Benefits

Improved disease-free survival and overall survival

Potential Harms

Toxicity associated with chemotherapy and radiation therapy (RT) (e.g., cardiovascular complications, secondary malignant neoplasms [SMN], myelosuppression, infertility)

See the original guideline document for more information on potential harms of treatment.

Qualifying Statements

Qualifying Statements

- The American College of Radiology (ACR) Committee on Appropriateness Criteria (AC) and its expert panels have developed criteria for determining appropriate imaging examinations for diagnosis and treatment of specified medical condition(s). These criteria are intended to guide radiologists, radiation oncologists, and referring physicians in making decisions regarding radiologic imaging and treatment. Generally, the complexity and severity of a patient's clinical condition should dictate the selection of appropriate imaging procedures or treatments. Only those examinations generally used for evaluation of the patient's condition are ranked. Other imaging studies necessary to evaluate other co-existent diseases or other medical consequences of this condition are not considered in this document. The availability of equipment or personnel may influence the selection of appropriate imaging procedures or treatments. Imaging techniques classified as investigational by the U.S. Food and Drug Administration (FDA) have not been considered in developing these criteria; however, study of new equipment and applications should be encouraged. The ultimate decision regarding the appropriateness of any specific radiologic examination or treatment must be made by the referring physician and radiologist in light of all the circumstances presented in an individual examination.
- ACR seeks and encourages collaboration with other organizations on the development of the ACR AC through society representation on expert panels. Participation by representatives from collaborating societies on the expert panel does not necessarily imply individual or society endorsement of the final document.

Implementation of the Guideline

Description of Implementation Strategy

An implementation strategy was not provided.

Institute of Medicine (IOM) National Healthcare Quality Report Categories

IOM Care Need

Getting Better

Living with Illness

IOM Domain

Effectiveness

Identifying Information and Availability

Bibliographic Source(s)

Roberts KB, Younes A, Hodgson DC, Advani R, Dabaja BS, Dhakal S, Flowers CR, Ha CS, Hoppe BS, Mendenhall NP, Metzger ML, Plastaras JP, Shapiro R, Smith SM, Terezakis SA, Winkfield KM, Constine LS, Expert Panel on Radiation Oncologyâ€“Lymphoma. ACR Appropriateness CriteriaÂ® Hodgkin lymphoma - unfavorable clinical stage I and II. Reston (VA): American College of Radiology (ACR);

2015. 22 p. [83 references]

Adaptation

Not applicable: The guideline was not adapted from another source.

Date Released

2015

Guideline Developer(s)

American College of Radiology - Medical Specialty Society

Source(s) of Funding

The American College of Radiology (ACR) provided the funding and the resources for these ACR Appropriateness Criteria®.

Guideline Committee

Committee on Appropriateness Criteria, Expert Panel on Radiation Oncology–Lymphoma

Composition of Group That Authored the Guideline

Panel Members: Kenneth B. Roberts, MD (*Principal Author*); Anas Younes, MD (*Co-author*); David C. Hodgson, MD (*Panel Vice-chair*); Ranjana Advani, MD; Bouthaina S. Dabaja, MD; Sughosh Dhakal, MD; Christopher R. Flowers, MD, MS; Chul S. Ha, MD; Bradford S. Hoppe, MD, MPH; Nancy P. Mendenhall, MD; Monika L. Metzger, MD; John P. Plastaras, MD, PhD; Ronald Shapiro, MD; Sonali M. Smith, MD; Stephanie A. Terezakis, MD; Karen M. Winkfield, MD, PhD; Louis S. Constine, MD (*Panel Chair*)

Financial Disclosures/Conflicts of Interest

Not stated

Guideline Status

This is the current release of the guideline.

This guideline updates a previous version: Das P, Ng A, Constine LS, Advani R, Flowers C, Friedberg J, Hodgson DC, Schwartz CL, Wilder RB, Wilson LD, Yunes MJ, Expert Panel on Radiation Oncology-Hodgkin's Lymphoma. ACR Appropriateness Criteria® Hodgkin's lymphoma - unfavorable clinical stage I and II. [online publication]. Reston (VA): American College of Radiology (ACR); 2010. 6 p. [24 references]

This guideline meets NGC's 2013 (revised) inclusion criteria.

Guideline Availability

Available from the American College of Radiology (ACR) Web site .

Availability of Companion Documents

The following are available:

- ACR Appropriateness Criteria®. Overview. Reston (VA): American College of Radiology; 2015 Oct. 3 p. Available from the American College of Radiology (ACR) Web site.
- ACR Appropriateness Criteria®. Literature search process. Reston (VA): American College of Radiology; 2015 Feb. 1 p. Available from the ACR Web site.
- ACR Appropriateness Criteria®. Evidence table development. Reston (VA): American College of Radiology; 2015 Nov. 5 p. Available from the ACR Web site.
- ACR Appropriateness Criteria®. Topic development process. Reston (VA): American College of Radiology; 2015 Nov. 2 p. Available from the ACR Web site.
- ACR Appropriateness Criteria®. Rating round information. Reston (VA): American College of Radiology; 2015 Apr. 5 p. Available from the ACR Web site.
- ACR Appropriateness Criteria® Hodgkin lymphoma—unfavorable clinical stage I and II. Evidence table. Reston (VA): American College of Radiology; 2015. 43 p. Available from the ACR Web site.
- ACR Appropriateness Criteria® Hodgkin lymphoma—unfavorable clinical stage I and II. Literature search. Reston (VA): American College of Radiology; 2015. 1 p. Available from the ACR Web site.

Patient Resources

None available

NGC Status

This NGC summary was completed by ECRI Institute on May 16, 2007. This summary was updated by ECRI Institute on December 23, 2010. This summary was updated by ECRI Institute on February 12, 2016.

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